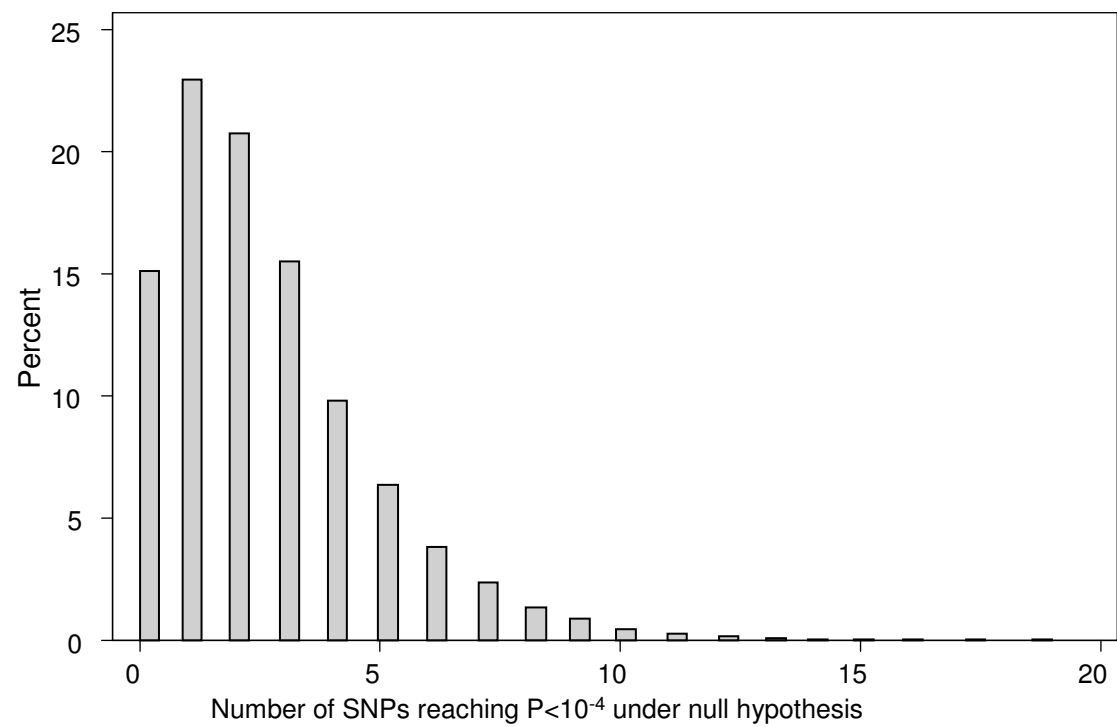**Figure S2. Simulated distribution of P values from discovery stage meta-analyses.**

a) Determination of replication threshold

The distribution of the number of SNPs with a P value$<10^{-4}$ under the null hypothesis of no associated SNPs is based on 50,000 simulations using the controls from the BHF-FHS study. The median is 2 significant SNPs (mean 2.5), suggesting that using this threshold for taking SNPs to the replication stage is likely to result in few false positives. The comparable numbers for a threshold of P$<10^{-3}$ are median=27 (mean 27), whilst the mean was 0.25 for P$<10^{-5}$.

b) Chip-wide significance threshold
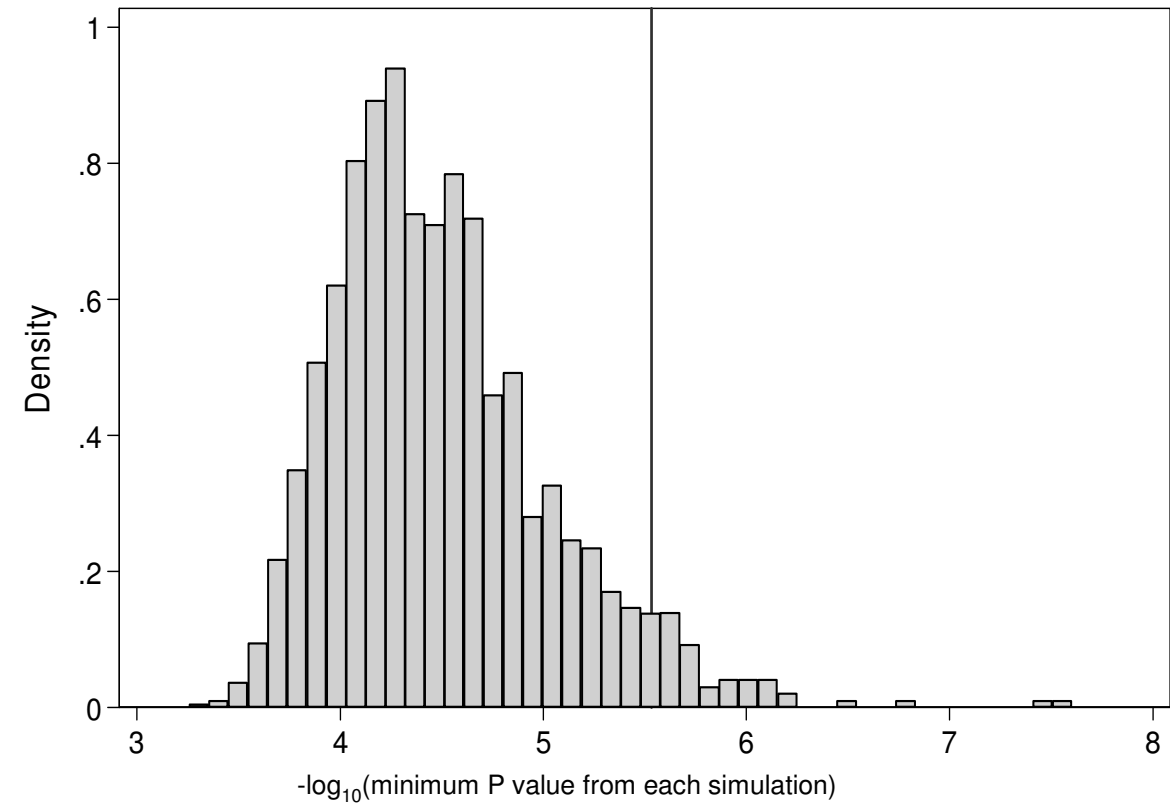
The distribution of lowest P value in each simulation across the Human CVD Beadchip array is based on 50,000 simulations using the controls from the BHF-FHS study. The vertical line at P=3×10^{-6} represents the 5th percentile, which was selected to denote chip-wide significance.